

Appl. No. 10/598,149  
Amdt. dated April 2, 2009  
Reply to Office Action of October 3, 2008

**Amendments to the Drawings:**

The attached sheets of drawings includes changes to Fig. 3 and Fig. 6. These sheets, which include Figs. 3, 4 and 6, replace the original sheets including Figs. 3, 4 and 6.

Attachment: Two Replacement Sheets

## **REMARKS/ARGUMENTS**

With this response claims 1- 5, 16-20, 23 and 24 are pending. Claims 1, 4, 16, 20 are currently amended. Claims 21 and 22 are canceled. Claims 6-15 are withdrawn as drawn to a non-elected invention.

Applicants reserve the right to pursue, without prejudice, any subject matter including claim(s) as originally filed and/or otherwise set forth or described in this present application and/or in an earlier or other application(s) such as a priority application(s). No new matter is added.

## **SPECIFICATION AMENDMENTS**

The Office objects to the specification “because trademarks are disclosed throughout the instant specification and not all of them are capitalized or accompanied by the generic terminology.” The Office points to the use of TALON in paragraph [0052], page 4 of the published patent application. In the interest of facilitating prosecution, Applicants submit herewith a replacement paragraph (corresponding to paragraph [0054], page 12 of the PCT application as-filed) where the term TALON is identified as a trademark by the use of the common law trademark symbol TM (e.g., TALON<sup>TM</sup>). This amendment does not introduce new matter.

## **CLAIM AMENDMENTS**

Solely in order to facilitate prosecution, claims 1, 4, 16 and 20 are amended to recite the sequence contained in SEQ ID NO:3. Support for this amendment is found throughout the application, such as in original claim 3 and at paragraphs [018] – [019] and the table provided therein.

For clarity “at position 388” in claims 1 and 4 is deleted as redundant, as SEQ ID NO:3 explicitly contains a substitution of Leucine for methionine (see position 40). That substitution corresponds to position 388 of the EGF (4-6) like domains, as summarized in Scheme A of Fig. 1.

In view of the amendments, claims 21 and 22 are canceled as redundant.

No new matter is added with this amendment, and entry of the claims presented herein is respectfully requested.

### **DRAWINGS**

The Office notes the application contains drawings executed in color (Fig. 3) and requires applicant to file a petition. Applicant submits herewith amended Fig. 3 on a replacement sheet in accordance with Office rules that is not in color. In addition, Applicant notes Fig. 6 was previously executed in color and submits herewith amended Fig. 6 not in color. Accordingly, the revised drawings delete reference to the color portion. The amendment does not constitute the addition of new matter. Applicants request the replacement sheets be entered and that the requirement for a petition be withdrawn.

### **CLAIM REJECTIONS – 35 U.S.C. § 112**

#### **ITEM 7**

The Office rejects claims 1-2, 4-5 and 16-24 under 35 U.S.C. 112, first paragraph and alleges they contain “subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.” Applicants respectfully traverse this rejection in view of the amendments and remarks presented herein.

In support of this rejection, the Office alleges the “claims lack structural information.” The pending independent claims recite SEQ ID NO:3. Given the structural information explicitly contained in SEQ ID NO:3, Applicants believe the 35 U.S.C. 112 rejection is obviated and, accordingly, request reconsideration and withdrawal of this rejection.

#### ITEM 8

The Office rejects claims 1-5 and 16-24 under 35 U.S.C. 112, first paragraph, alleging the specification “while being enabling for the proteins set forth in SEQ ID NO:3, does not reasonably provide enablement for any truncated thrombomodulin protein comprising SEQ ID NO:3 or any thrombomodulin derivative or any polymer conjugated to the same.” Applicants respectfully traverse this rejection.

First, the claims presented herein all comprise SEQ ID NO:3. As noted in the specification of the present application, proteins containing SEQ ID NO:3, including a protein that is a conjugate of SEQ ID NO:3 and a polymer, has thrombomodulin bioactivity (see, e.g., “EXAMPLE 1. C-terminal site-specific PEGylation of a truncated thrombomodulin with full bioactivity” at paragraphs [045], page 9 – [0075], page 18). As stated in the specification:

A human thrombomodulin derivative containing EGF(4-6)-like domains designed with an azido-functionalized methionine C-terminal linker was successfully synthesized using a genetic engineering strategy. The protein exhibited bioactivity towards protein C that was comparable to native human TM. Paragraph [0074], page 18.

Furthermore, the specification states: “Enzyme activity before and after PEGylation was substantially similar indicating the utility and successful application of the site-specific PEGylation method.” Page 18, lines 12-14.

Accordingly, the SEQ ID NO:3 portion of a protein provides thrombomodulin bioactivity, and the remaining portions of the protein or conjugated protein comprising SEQ ID NO:3 do not substantially affect that bioactivity. Furthermore, a polymer conjugated to the protein comprising SEQ ID NO:3 maintains thrombomodulin bioactivity, as explicitly shown in Example 1 of the specification. Applicants assert the specification does, in fact, enable any person skilled in the art to which the claims pertain, to make the invention commensurate in scope with pending claims, particularly in view of the fact that the pending claims recite SEQ ID NO:3.

As the pending claims all recite SEQ ID NO:3 in its entirety, the claimed invention does provide a clear and focused structural limitation.

The Office alleges “claim 3 encompasses fragments of SEQ ID NO:3.” See sentence spanning pages 6-7 of the Office Action. Clarification is respectfully requested as Applicants believe claim 3 (and the other independent claims) relates to proteins containing the entirety of SEQ ID NO:3 (e.g., from amino acid 1 to amino acid 144), and not proteins that only have a portion thereof.

With respect to the Office’s allegation related to predictability, such as a single nucleotide or amino acid change in a sequence being capable of affecting biomolecule function (citing Wells, Biochemistry, vol. 29, 8509-8517, 1990), Applicants believe the recitation of SEQ ID NO:3 in the pending claims obviates this rejection. As discussed, SEQ ID NO:3 provides the protein or protein-conjugate functionality as well as a clear structural limitation. Accordingly, as SEQ ID NO:3 provides functionality and structural limitations, Applicant believes the pending claims satisfy the requirements of 35 U.S.C. 112 and request the 112 rejections be reconsidered and withdrawn.

#### ITEM 9

The Office rejects claims 1-2 and 4-5 under 35 U.S.C. 112 as allegedly indefinite for the recitation of “position 388” absent a reference sequence. In view of the amendment to claims 1 and 4, where SEQ ID NO:3 is explicitly recited, and “at position 388” is deleted as redundant in view of SEQ ID NO:3 having a Met-388-Leu substitution at position 40, Applicants request this rejection be reconsidered and withdrawn.

### **CLAIM REJECTIONS – 35 U.S.C. § 102**

The Office rejects claim 16 under 35 U.S.C. 102(e), citing U.S. Pat. No. 7,250,168 (Light et al.). In view of the amendment to claim 16 that recites a conjugate comprising SEQ ID NO:3, Applicants believe this rejection is obviated as Light et al. does not teach or suggest SEQ ID NO:3. Applicants respectfully request this rejection be reconsidered and withdrawn.

### **CONCLUSION**

In view of the forgoing, Applicants believe the claims are in condition for allowance and respectfully requests the case be passed to allowance. If any outstanding issues remain, the Office is encouraged to contact the undersigned by telephone.

It is believed that the present submission requires the payment of a three month extension of time fee. The payment is being submitted herewith by the EFS-web system. If the payment is in an incorrect amount or missing any other fees, or if there is a problem with the EFS-web payment, please charge any fees required, including any extensions of time required, or credit any overpayment, to Deposit Account No. 07-1969.

Respectfully submitted,

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